

AMENDMENTS

In the Specification

Please replace the paragraph on page 2, lines 13-15, with the following:

B1 --Cyclic 3',5'-phosphate esters of araA, araC and thioinosine have been synthesized. Meyer *et al.*, *J. Med. Chem.* 22: 811-815 (1979). These compounds are ring-opened through the action of phosphodiesterases, which usually require one negative charge.--

Please replace the paragraph on page 4, lines 1-21, with the following:

B2 --A variety of substituted 1',3'-propanyl cyclic phosphoramidates, wherein 1' represents the carbon alpha to the nitrogen, were prepared as cyclophosphamide analogs (Zon, *Progress in Med. Chem.*, 19, 205 (1982)). For example, a number of 2'- and 3'-substituted proesters were prepared in order to decrease the propensity of the α,β -unsubstituted carbonyl by-product to undergo a Michael reaction. 2'-substituents included methyl, dimethyl, bromo, trifluoromethyl, chloro, hydroxy, and methoxy, whereas a variety of groups were used at the 3'-position, including phenyl, methyl, trifluoromethyl, ethyl, propyl, i-propyl, and cyclohexyl. Analogs with a 3'-aryl group (*e.g.* trans-4-phenylcyclophosphamide) were "moderately effective in L1210- test system and showed no activity *in vivo*." G. Zon, *Prog. Med. Chem.*, 19: 205-246 (1982). A variety of 1'-substituted analogs were also prepared. In general, these compounds were designed to be "pre-activated" cyclophosphamide analogs that bypass the oxidation step by already existing as a 1'-substituted analog capable of producing the final compound, *e.g.* hydroperoxide and 1-thioether. A series of 1'-aryl analogs were also prepared in order to enhance the oxidation potential. In contrast to the 1'-hydroperoxy analogs, the 1'-aryl compounds exhibited either no activity or very poor activity in the standard anticancer *in vivo* screen assay, *i.e.* the mouse L1210 assay. The lack of activity was postulated to arise from the steric hindrance of the phenyl and, therefore, limited oxidation of the prodrug. Support for this postulate was the potent activity of the acyclic phenyl keto analog, which exhibited activity similar to cyclophosphamide. Ludeman *et al.*, *J. Med. Chem.* 29: 716 (1986).--